81270V/47 B07 BEEC 05.05.73
BEECHAM GROUP LTD DT 2421-273
07.12.73-GB-056858 (+021502) (14.11.74) A61k-09 A61k-21

Direct compression tablet compositions - contg. 10-85 wt.% heavy basic magnesium carbonate and 5-85 wt.% active ingredient

Tablets contg. (a) 10-85 wt.% heavy basic magnesium carbonate, (b) 5-85 wt.% active ingredient, and (c) 0-40 wt.% usual tabletting adjuvants are new.

ADVANTAGES

The tablets can be produced by direct compression, and they possess the pH-regulating properties of heavy magnesium carbonate, giving better dissolution of acid-insoluble drugs.

DETAILS

Heavy basic magnesium carbonate (British Pharmacopoeia) corresponds approximately to the formula $3MgCO_3.Mg(OH)_2.4H_2O$. Anhydrous magnesium carbonate $MgCO_3$ is unsuitable because it is insufficiently compressible, and light basic magnesium carbonate ($3MgCO_3.Mg(OH)_2.3H_2O$) is unsuitable because of its unfavourable flow properties. Active ingredients which are suitable for inclusion in the tablets include therapeutically active organic compounds or their mixtures (with the exception of acetylsalicylic acid), e.g. antiulcer, anti-inflammatory or anti-hypertensive agents, antihistamines, vitamins, penicillins, cephalosporins or other usual medicaments. Tabletting adjuvants which can be included include lubricants, preservatives, dyes, flavouring, fillers, binding agents, solid organic acids, etc.

Preferred tablets contain 30-85 wt.% of a β-lactam antibiotic, 10-70 wt.% of heavy basic magnesium carbonate and 0-40 wt.% tabletting adjuvants. The β-lactam antibiotic can be in the form of a salt or ester, and is pref. only slightly soluble (< 3%) soluble in aqueous HCl at pH 1.3 and 37°C. The tablets are produced simply by mixing the ingredients and compressing the mixture (pref. by direct compression).

EXAMPLE

1% polyvinylpyrrolidone-coated phenethicillin microcapsules are directly compressed at 820 kg./cm² in the following mixture: 49 wt.% phenethicillin microcapsules (250 mg. phenethicillin), 39 wt.% heavy basic magnesium carbonate, 2 wt.% Mg stearate, 8 wt.% disintegrating agent, 2 wt.% sodium laurylsulphate. 50% dissolution of the tablets is obtained within 7.5 mins. at pH 1.5, 37°C and 60 rpm. When the phenethicillin and magnesium carbonate are replaced by 88% phenethicillin microcapsules, the dissolution time under the same conditions is 12.5 mins. Both mixtures are equally suitable for direct compression. 81270V

81290V/47 B05-(B04) THER- 24.01.73
LAB THERANOL FR 2215-201
24.01.73-FR-002390 (27.09.74) A61k-21

Broad-spectrum antibiotic compsns. - contg. antibiotic resistant lactic bacilli and enzyme diffusing-agent

Therapeutic compns. comprising a broad-spectrum antibiotic, e.g. tetracyclines or chloramphenicol, and a culture of lactic bacilli resistant to the antibiotics, together with an enzyme diffusing-agent, especially hyaluronidase or lysozyme.

USE

The antibiotic compns. are less liable to induce side-effects following adventitious destruction of normal intestinal flora.

DETAILS

In addition to the pref. enzymes, proteases may be used. Pref. cultures are freeze-dried cultures of Lactobacillus acidophilus resistant to tetracyclines, penicillin, neomycin, chloramphenicol, erythromycin and cathomycin. The unit doses contain 100-250 mg. antibiotic; 6-15 mg. enzyme and at least 500 million living bacilli.

EXAMPLE

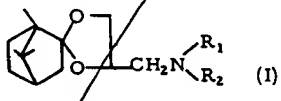
A compn. contained tetracycline hydrochloride 150 mg, lysozyme hydrochloride 10 mg, a freeze-dried culture of L. acidophilus resistant to antibiotics, especially tetracycline containing 500 x 10^6 organisms. This formed a single unit dose.

81290V

81291V/47 B03 DELL 18.03.71
DELALANDE SA FR 2215-205
04.01.73-FR-000250 (+009448) (27.09.74) A61k-27 C07d-13/04 C07d-99/04

Amino methyl norbornane spiro dioxolanes - having positive inotropic, hypotensive anti-inflammatory, diuretic CNS stimulant, etc. activity

Compounds of formula (I) are new:



(I)

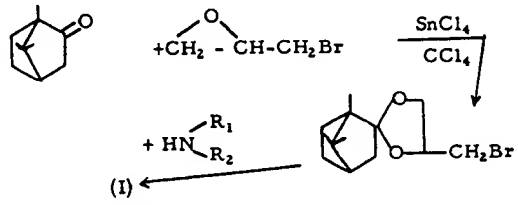
(where $-NR_1R_2$ = monoalkylamino (1-4C), or piperazino substituted in the 4-position either by alkyl (1-4C) or by an aminocarbonylmethyl group $-CH_2CON<$ where $N<$ is dimethylamino, pyrrolidino, morpholino or hexamethyleneimino).

This is an Addition to 7109448.

USE

The compounds have positive inotropic, vasodilating, anti-inflammatory, spasmolytic, diuretic, antiulcer activity.

The compounds are prepd. by the same method as described in the parent patent, i.e.



ADMINISTRATION

The compounds may be given orally as tablets etc., contng. 50-400 mg. (I) (3-5 per day), as a liquid contng. 0.5-2% (I) (10-50 drops, 3 times daily) as an injectable ampoule contng. 10-100 mg. (I) (1-3 times per day), or rectally as suppositories contg. 40-300 mg. (I) (1 or 2 times per day).

TOXICITY

The oral LD_{50} of a number of compounds of formula (I) was measured and varied between 625 mg/kg ($NR'R^2$= 4-(dimethylaminocarbonylmethyl)piperazino) and 2600 mg/kg.

81291V Contd